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Regina D. McKinney

June 4, 2004

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Re: Appl. No. 09/966,893; Filed: September 28, 2001
For: TARGETING PROTEINS FOR CELLS EXPRESSING MANNOSE RECEPTORS VIA EXPRESSION IN INSECT CELLS
Inventors: Alessandra D'Azzo, *et al*
Our Ref: SJ-01-0020
Customer Number : 28258

Sir:

The following documents are forwarded herewith for appropriate action by the U.S. Patent and Trademark Office:

1. Reply Brief Pursuant to 37 C.F.R. § 1.193(b) (7 pgs.); and

2. A self-addressed and stamped return postcard

Regards,

J. Scott Elmer
Reg. No. 36,129
Director, Office of Technology Licensing

Enclosures (2)

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Regina D. McKinney

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	:	
D'Azzo *et al.*	:	Art Unit: 1652
Serial No. 09/966,893	:	Examiner: Christian l. Fronda
Filed: September 28, 2001	:	Atty Docket: SJ-01-0020
For: Targeting Proteins to Cells Expressing Mannose Receptors Via Expression in Insect Cells	:	

REPLY BRIEF PURSUANT TO 37 C.F.R. §1.193(b)

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

This is an Appeal from the Final Rejection of claims 8-13 of the referenced application (published on June 20, 2002 as Pub. No. 2002/0077292) dated July 1, 2003. The Examiner subsequently issued an Advisory Action dated December 2, 2003 upholding this rejection. The Notice of Appeal was filed for this application on September 5, 2003, and an Appeal Brief was timely filed on December 10, 2003 with a petition for a two-month extension of time. An Examiner's Answer was mailed April 20, 2004 and received on April 26, 2004. The following reply is in response to specific points raised in the Examiner's Answer and is timely submitted within two months from the date of the Examiner's Answer.

No fee is believed to be required for this submission. If Appellants are incorrect and a fee is required the Commissioner is hereby authorized to charge such fee to Deposit Account No. 501968.

I. The claims are limited in scope to proteins listed in Table 1

Appellants have noted that Table 1 provides a comprehensive list of proteins useful for treating lysosomal storage disorders (LSDs; see Appeal Brief at page 7, par. 2). Appellants have also attempted to amend claim 8 to include only proteins listed in Table 1. Thus Appellants have clearly documented their intent to interpret the phrase "proteins useful for treating lysosomal storage disorders (LSDs)" in claim 8 (and claims depending from this claim) to encompass only those proteins listed in Table 1 of the specification.

In spite of Appellants clear intent, the Examiner maintains that the claims must be interpreted to cover additional proteins because they "must be given their broadest reasonable interpretation consistent with the specification." Examiner's Answer at page 14, par. 2; *see also* page 21, par. 2. Appellants disagree for two reasons. First, the Examiner has failed to identify any specific proteins other than those listed in Table 1 that would be included in the scope of the claims, nor are Appellants aware of any such proteins. Thus the Examiner has failed to establish that the broadest reasonable interpretation of these claims would include any proteins other than those listed in Table 1.

While not identifying any specific proteins, the Examiner does speculate on page 15 of the Examiner's Answer that there are "many other proteins not listed in Table 1 of the specification useful for just treating symptoms of any lysosomal storage disorder but not curing the lysosomal storage disorder, whether or not the protein directly replaces a deficiency or treats the symptoms of the lysosomal storage disorder." Appellants are unaware of what proteins the Examiner refers to in this statement. Appellants further submit that the inclusion of any such proteins in the scope of the claims clearly represents an overly broad and unreasonable

interpretation of the claims in view of the prosecution history and the specification, which describes only proteins that replace deficiencies associated with LSDs as useful for treating LSDs.

Appellants also cannot agree with the Examiner because he is applying the requirement under MPEP §2111 to give claims their broadest reasonable interpretation in a way which vitiates the right of a patent applicant to act as their own lexicographer. The Examiner is using this requirement as a reason to ignore Appellants clear intent with respect to the interpretation of the claims. Appellants respectfully submit that this constitutes an unreasonable and improper application of this requirement. Instead, a patent applicant's clear intent to give claims a particular meaning should be respected and taken into account when applying this requirement. Thus, an interpretation of a claim term which is broader than the meaning clearly attributed by the patent applicant should not be considered "reasonable" when applying this "broadest reasonable interpretation" standard.

MPEP §2111 notes that "Applicant always has the opportunity to amend claims during prosecution" as a way of addressing a claim interpretation that is considered overly broad. In this case, however, Appellants were not allowed to amend the claims in a manner consistent with their interpretation. Thus Appellants have been placed in an untenable position in which they have not been allowed to amend the claims to reflect their intended meaning and their intended meaning has been disregarded by the Examiner when interpreting the claims.

II. Limiting the scope of each listed protein to a specific amino acid sequence is not necessary to satisfy the written description requirement

The Examiner also asserts that the claims fail to meet the written description requirement because they include variants of named proteins. This is most apparent from the rejection of claim 10, which is limited to protective protein/cathepsin A (PPCA). Despite this limitation, this claim is not sufficiently described according to the Examiner because it "includes many PPCA proteins

with widely differing structural, chemical, and physical characteristics, and the genus is highly variable because a significant number of structural differences between PPCA protein genus members is permitted." (Examiner's Answer at page 15, second full paragraph).

As Appellants have repeatedly noted, the primary structure (i.e. amino acid sequence) of proteins included in the claimed compositions are well known in the art. This certainly includes PPCA whose amino acid sequence is deposited as Genbank accession number M22960 (see Table 1 of the application disclosure).

It is well within the capabilities of the ordinary skilled artisan to make variations in the primary structure of the PPCA protein, as well as other proteins within the claimed compositions, and retain the fundamental function and identity of these proteins. Appellants do not agree that such protein variants would have widely differing structural, chemical and physical characteristics, but submit that such variants represent minor changes which do not affect the function of the protein. Moreover, Appellants submit that a specific description of all such variants is not necessary to sufficiently describe the claimed compositions since such variants can be made by the ordinary skilled artisan with no further teaching or guidance. If such a specific description of all encompassed variants were necessary, most if not all existing patent claims to compositions comprising proteins which are identified according to their name rather than to a specific amino acid sequence would fail to satisfy the written description requirement since no such patent Appellants are aware of provide an exhaustive recitation of all possible variants of the named protein. For example, claim 4 of U.S. Patent No. 5,658,567 (Document AB1 made of record during prosecution) claims in part "A pharmaceutical composition comprising a pharmaceutically effective amount of recombinant glycosylated biologically active alpha.-galactosidase". However, this patent fails to recite all possible variants which would constitute "biologically active alpha-galactosidase", including single and multiple amino acid substitutions or additions and deletions, truncates, etc. Instead, as with the present disclosure this patent relies

upon the knowledge and skill in the art which those in the field recognize as placing such variants in the possession of the patentee without their specific recitation.

In addition, Appellants note that such variation in the primary structure of proteins encompassed by the claims is not relevant to the inventive aspect of these compositions, which relates to the method in which these proteins are produced irrespective of their specific structure. In other words, it is not the amino acid sequence of the claimed compositions which Appellants assert to be new and nonobvious, but rather other properties of these compositions which arise by virtue of the way in which they are produced.

III. Steps asserted to require undue experimentation are not required to practice of the claimed invention

On page 22 of the Examiner's Answer, the following steps are asserted to require undue experimentation:

1) performing tests on a patient to determine and confirm whether a patient has any LSD;
2) ascertaining the etiology of the disease; and
3) searching and screening for a protein useful in the form of a pharmaceutical composition to treat the patient without harming them.

The present invention is drawn to a class of pharmaceutical compositions comprising known proteins, many of which have already been used clinically (see paragraphs 0010-0034 of Pub. No. 2002/0077292), for treating known conditions. None of the noted steps are required to make and use these compositions and thus the issue of whether undue experimentation is required to practice these steps is not relevant to the issue of whether the claimed compositions are enabled. The protein component of the claimed compositions and the LSDs they are associated with are well known; no search is necessary. With respect to use, Appellants note that use of the claimed compositions presupposes the identification of the relevant patient population suffering from a

lysosomal storage disorder, just as a claim to a composition for treating leukemia would presuppose the identification patients suffering from leukemia. In both cases the identification of the relevant patient population is a known prerequisite rather than a step that must be taught to enable the claimed composition. To the extent that the Examiner intends to assert that it is not within the level of skill in the art to routinely identify specific LSDs, Appellants disagree and note that the Examiner has failed to support such an assertion with any evidence.

IV. New grounds of rejection for anticipation are improper and should fail

Prior to the Examiner's Answer, the Sharp reference was NOT asserted by the Examiner to teach a pharmaceutical composition for treating Galactosialidosis comprising a PPCA polypeptide produced in an insect cell culture. For the first time in the Examiner's Answer Sharp is asserted to provide such a teaching. *See* Examiner's Answer at page 28, second full paragraph. In addition to improperly introducing a new ground of rejection, Appellants submit that Sharp fails to teach a PPCA polypeptide produced in an insect cell culture for treating Galactosialidosis.

As noted in the Appeal Brief, Sharp does generically mention the production of proteins in insect cells when providing a laundry list of the various forms of standard expression vectors and host cells that may be used to produce proteins (see Sharp at pages 65-72, particularly 66-67). However, Sharp does not specifically teach the production of PPCA (i.e TANGO 176) in insect cell culture for the purpose of making a pharmaceutical composition useful for treating Galactosialidosis. Nor can such a teaching be inferred, as the Examiner has done, considering the state of the art at the time of the Sharp disclosure. Appellants have explained that proteins produced in insect cells had ill-defined properties which made them unattractive for therapeutic purposes at the time of the Sharp disclosure. Viewed in light of the state of the art, the disclosure of Sharp would not have conveyed to the skilled artisan the specific idea of producing PPCA in an insect cell for the purpose of producing a pharmaceutical composition useful for treating

Galactosialidosis. This idea is only apparent from the application disclosure which is the subject of this appeal.

V. Conclusion

Appellants maintain that all outstanding rejections should be reversed for the reasons set forth in their Appeal Brief as supplemented by the remarks above addressing specific points of argument raised in the Examiner's Answer.

Respectfully submitted,

James Scott Elmer
Attorney for Applicant
Registration No. 36,129

St. Jude Children's Research Hospital
332 North Lauderdale
Memphis, TN 38105-2794
Telephone: 901-495-2756

Date: June 4 2004